UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte CHARLES L. SHEAR

Appeal No. 2006-0819
Application No. 09/929,862

ON BRIEF

Before SCHEINER, GRIMES, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 4, 5 and 8-14. Claim 1 is drawn to a composition comprising [2R, 4S]4-[(3,5-bis-trifluoromethyl-benzyl)-methoxycarbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester (a CETP inhibitor compound), certain hydroxy metabolites (or their salts) of atorvastatin,[1] and a pharmaceutically acceptable carrier, vehicle or diluent.

[1] See Appeal Brief, page 3. Note that all references to the Appeal Brief are to the "brief on Appeal," filed August 10, 2005, and stamped August 12, 2005. The claimed hydroxy metabolites or their salts of atorvastatin are derivatives of Lipitor®, which is atorvastatin calcium.

Claim 5 is drawn to "[a] method for slowing the progression of atherosclerotic plaques, causing the regression of atherosclerotic plaques or managing cardiac risk, or treating atherosclerosis, hyperlipidemia, HDL elevation or angina in a mammal in need of therapeutic treatment comprising administering to said mammal a therapeutically effective amount" of the composition of claim 1.

Claims 1, 4, 5 and 8-14 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Deninno[2] and Roth.[3] After careful review of the record and consideration of the issue before us, we affirm.

BACKGROUND

According to the specification, "[t]he conversion of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) to mevalonate is an early and rate-limiting step in the cholesterol biosynthetic pathway. This step is catalyzed by the enzyme HMG-CoA reductase. Statins inhibit HMG-CoA reductase from catalyzing this conversion. As such, statins are lipid lowering agents." Id. at 1. Atorvastatin calcium, currently sold as Lipitor®, is one such statin. See id. at 2.

Cholesteryl ester transfer protein (CETP) transfers cholesteryl ester and triglyceride between lipoprotein particles, including high density lipoproteins (HDL), low density lipoproteins (LDL), very low density lipoproteins (VLDL), and chylomicrons. See id. at 4. CETP activity results in lowering HDL cholesterol, increasing LDL cholesterol, and is believed to be pro-atherogenic. See id.

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[2] Deninno et al. (Deninno), WO 00/17164, published March 30, 2000.
[3] Roth, U.S. Patent No. 4,681,893, issued July 21, 1987.

> [2R, 4S]4-[(3,5-Bis-trifluoromethyl-benzyl)-methoxycarbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester [a CETP inhibitor compound] is disclosed in PCT/IB99/01532 application published as WO 00/17164 on March 30, 2000 as a CETP inhibitor for the elevation of certain plasma lipid levels and to lower certain other plasma lipid levels and accordingly to prevent the occurrence of and treat diseases such as lipid abnormalities, atherosclerosis and cardiovascular diseases. That published application also discloses the combination of a genus of 4-carboxyamino-2-substituted-1,2,3,4-tetrahydroquinolines with a preferred group of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors being lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin or rivastatin.

Id. at 1.

DISCUSSION

As appellant does not argue the patentability of the claims separately, they stand or fall together, and we focus our analysis on claim 1.

Claims 1, 4, 5 and 8-14 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Deninno and Roth

Deninno is cited for teaching compositions for treating conditions such as atherosclerosis through the administration of a composition that may comprise [2R, 4S]-4-[(3,5-bis-trifluoromethyl-benzyl)-methoxycarbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester and a HMG-CoA reductase inhibitor, which may be atorvastatin. See Examiner's Answer, pages 2-3. According to the examiner, "[t]he difference between the above and the claimed subject matter lies in that Deninno [ ] only highlights atorvastatin and fails to teach the presently claimed salts and/or hydroxy acid forms thereof." Id. at 3.

The examiner, however, concludes:

> [T]he difference between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because Roth teaches the presently claimed salt forms and hydroxyl acid forms of atorvastatin . . . as being effective [sic] HMG-CoA reductase inhibitors and the skilled artisan would have been motivated to alternatively use these compounds of Roth for the purpose taught by Dennino [ ] for atorvastatin because not only was it known that atorvastatin (see Dennino [ ] as referenced above) and the presently claimed salt forms and hydroxy acid forms of atorvastatin were known to function as HMG-CoA-reductase inhibitors (see Roth as referenced above), but Dennino [ ] teach that HMG-CoA reductase inhibitors in general could be combined with [2R, 4S] 4-[(3,5-bis-trifluoromethyl-benzyl)-methoxycarbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester for the purposes taught therein and presently claimed.

Id. at 3

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant." In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993) (citations omitted). The test of obviousness is "whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention." In re Gorman, 933 F.2d 982, 986, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). We conclude that the examiner has met the burden of establishing a prima facie case of obviousness, and the rejection is affirmed.

Appellant argues that the examiner has failed to make out a prima facie case of obviousness. See Appeal Brief, page 6. Appellant asserts, relying on In re Geiger, 815 F.2d 686, 688 2 USPQ2d 1276, 1278 (Fed. Cir. 1987), "[w]hile each of these individual drugs was known per se and was used alone for certain medicinal purposes . . . their specific use together in a fixed composition has not been described in the prior art cited by the Examiner for any reason whatsoever." Id. Geiger, according to appellant, supports the proposition that even though three separate ingredients each had been used separately for the same purpose, it would have only been obvious to try combinations of those agents. See id. Thus, "[w]hile both the atorvastatin metabolite and 'the CETP inhibitor compound' are used in the treatment of various heart conditions, their specific applications and mechanisms of action are quite different," and thus there is no motivation, as in Geiger, to arrive at the claimed combination. Id. at 7.

Moreover, appellant asserts, "there is no teaching or suggestion in the art that these particular drugs should be selected from the vast array of available compounds and combined in a single pharmaceutical composition," and at most, the art only supports an "obvious to try" situation. Id. (emphasis in original). Appellant asserts that there must be a reason suggested by the references, and not hindsight, to select the claimed components and put them together in a single pharmaceutical composition. See id. "Specifically, Deninno [ ] recites a whole host of specific CETP inhibitors and embraces a genus of an even greater

number of CETP inhibitors," and "Roth teaches a vast amount of HMG-Co A reductase inhibitors in addition to the hydroxy metabolites of atorvastatin." Id. Appellant contends that "there is simply no direction to select these two specific compounds out of all the possible combinations of HMG-Co reductase inhibitors (Roth) and CETP inhibitors (Deninno)." Id. at 7-8.

Appellant's arguments are not found to be convincing. Deninno, although disclosing a large genus of compounds of Formula I, see id. at 2-6, specifically teaches the claimed species, i.e., [2R, 4S]-4-[(3,5-bis-trifluoromethyl-benzyl)-methoxycarbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester, see id. at 9, lines 25-26 and claim 6. Moreover, Deninno reasonably suggests the claimed composition. That is, Deninno teaches a pharmaceutical composition comprising a CETP inhibitor of Formula I and a second compound, which is preferably a HMG-CoA reductase inhibitor or a MTP/Apo B secretion inhibitor. See id. at 29, lines 21-32 and claims 39 and 40. Among the preferred HMG-CoA reductase inhibitors is atorvastatin. See id. at page 30 and claim 41. Thus, Deninno specifically teaches a composition comprising a CETP inhibitor of Formula I, wherein the claimed CETP inhibitor, i.e., [2R, 4S]-4-[(3,5-bis-trifluoromethyl-benzyl)-methoxycarbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester, is specifically taught by the reference, and a second compound comprising a HMG-CoA reductase inhibitor, with atorvastatin being preferred. Thus, there is a teaching or suggestion provided by the combination of references to select these

particular drugs and combine them into a single pharmaceutical composition. In addition, as noted by the examiner, Roth teaches the presently claimed salt forms and hydroxy acid forms of atorvastatin, and teaches that they are effective HMG-CoA reductase inhibitors, and thus the combination of Dennino and Roth teaches the presently claimed composition.

We therefore do not find Geiger to be on point, because as noted by appellant, that case dealt with the obviousness of the combination of three individually known components each known to be used for the same purpose. In this case, however, one of the references, Deninno, clearly provides a suggestion to arrive at the claimed combination by teaching a pharmaceutical composition comprising a CETP inhibitor and a HMG-CoA reductase inhibitor.

CONCLUSION

Because the examiner has set forth a prima facie case of obviousness, the rejection of claims 1, 4, 5 and 8-14 under 35 U.S.C. § 103(a) as being obvious over the combination of Deninno and Roth, is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

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Administrative Patent Judge)
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